Treatment Strategies for the Claudicant

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Abstract

Peripheral arterial disease (PAD) is a prevalent, morbid, and mortal disease. Claudication represents an early, yet common manifestation of PAD. A clinical history and physical examination combined with an ankle-brachial index can help make a diagnosis of claudication. Due to the polyvascular nature of the underlying atherosclerosis, PAD is often associated with heart disease and stroke. Although health implications of PAD derive from both its limb and cardiovascular manifestations, claudication is life-threatening, less limb-threatening. Medical modification of cardiovascular risk factors and exercise are the cornerstone in the treatment of claudication. Revascularization in claudication is focused at improvement in claudication symptoms and functional status, rather than aggressive attempts at limb salvage. The aim of this article is to summarize the strategies in the treatment of claudication, to serve as a concise and informative reference for physicians who are managing these patients. A framework of the decision-making process in the management of patients with claudication is shown, which can be applied in clinical practice.

Keywords
- peripheral arterial disease
- claudication
- risk factor modification
- exercise therapy
- revascularization
- interventional radiology

Objectives: Upon completion of this article, the reader will be able to (1) make a diagnosis of claudication; (2) discuss the role of medical management, exercise therapy, and revascularization in management; and (3) individualize therapy to the needs of the patient.

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Claudication (derived from the Latin word "claudicare," meaning to limp) is pain and/or cramping in the leg due to inadequate blood flow to the muscles; the pain usually causes the person to limp. Claudication represents an early, yet common manifestation of peripheral arterial disease (PAD), a prevalent, morbid, and mortal disease. While HIV is described as a pandemic with a prevalence of 34 million people, conservative estimate of the global burden of PAD is more than 202 million.[1,2]

Atherosclerosis of the large- and medium-size arteries is an important cause of PAD. Accumulation of lipid and fibrous material between the intimal and medial layers of the vessel causes luminal narrowing. Ischemic symptoms result when there is an imbalance between the supply and demand for blood flow due to this narrowing.[3] The clinical manifestations of PAD depend on the location and severity of arterial stenosis. About 10 to 20% of people with PAD have intermittent claudication, and another 50% have atypical leg symptoms.[4] At the other spectrum of PAD is critical limb ischemia, a serious condition that, left untreated, can lead to amputation and death.[5] It is important to note that in addition to limb symptoms, 61% of PAD patients have concomitant coronary artery disease and/or cerebrovascular disease pointing out to the polyvascular systemic nature of atherosclerosis causing the PAD.[6]

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The purpose of this review is to highlight treatment strategies for the claudicant, after making a diagnosis of PAD, and to develop a therapeutic algorithm that can be applied in the management of claudicant in a vascular and interventional radiology clinical practice.

Making a Diagnosis

Who Is at Risk?

Patients at risk for developing PAD are those who are older than 65 years, those with risk factors for atherosclerosis (e.g., diabetes mellitus, history of smoking, hyperlipidemia, and hypertension), family history of PAD, and individuals with known atherosclerotic disease in another vascular bed (e.g., coronary, carotid).[7,8]

How to Make a Clinical Diagnosis?

The diagnosis of "classic" claudication is based on a classic history of fatigue, discomfort, cramping, or pain in the muscles of the lower extremities that is consistently induced by exercise and consistently relieved by rest (within 10 minutes). Claudication presents when there is insufficient oxygen delivery to meet metabolic requirements of the skeletal muscles. While there are numerous classification schemes for PAD, the Rutherford classification[9] remains the most widely used in clinical practice.[10] "Classic" claudication has been described in the calf muscles, but can also involve the thigh, hip, and buttock. A large proportion of PAD patients also report atypical symptoms not consistent with classic claudication; 30 to 60% of patients report no exertional leg symptoms and approximately 45 to 50% report atypical leg symptoms.[11,12] Also other conditions such as nerve root compression, hip arthritis, symptomatic Baker's cyst, and venous disease may mimic the symptoms of claudication. In addition to symptoms, physical exam of absent or reduced peripheral pulses or the presence of audible bruits supports the diagnosis of claudication. However, it should be known that in some patients, this can manifest with normally palpable pulses and no bruits.[11]

Is Physiologic and Anatomic Testing Needed?

In patients with history or physical examination findings suggestive of PAD, the resting ankle-brachial index (ABI), with or without segmental pressures and waveforms, is recommended to establish the diagnosis. In patients at increased risk of PAD without the typical history and physical findings of PAD, performing ABI is reasonable[13] and can sometimes serve as a problem-solving tool. Although a low ABI (<0.9) supports the diagnosis,[14] a normal resting ankle-brachial pressure index (>0.9) does not rule out the diagnosis, especially if there is a high clinical suspicion. In these cases, an exercise ABI should be performed. In patients with calcified arteries, commonly diabetics, ABI can be falsely negative in which case a toe-brachial index (TBI) can be used. The TBI in a healthy patient should be 0.70 to 0.80.[15]

Invasive (angiography) and noninvasive anatomic testing (duplex ultrasound, CTA, or MRA) of the lower extremities is useful to diagnose anatomic location and severity of stenosis for patients with symptomatic PAD. However, these tools are often reserved for patients for whom revascularization is considered.[15] ►**Fig. 1** offers a basic approach to making a diagnosis of PAD. ►**Fig. 2** is the workup of a patient who presented with claudication.

Treatment Options for the Claudicant

Guiding Principles

- Patients with and without leg symptoms of PAD have roughly a threefold increase in risk of mortality and major cardiovascular (CV) events (heart attack and stroke) compared with those without PAD.[16]
- Claudicants have lower physical activity levels, higher rates of mobility loss, significantly greater functional limitations, and poorer quality of life than people without PAD.[17,18]
- Less than 5 to 10% patients with claudication ever progress to limb-threatening ischemia.[19,20]

Thus, it is important for a practicing vascular and interventional physician to recognize that although health implications of PAD derive from both its limb and CV manifestations, claudication is life-threatening, less limb-threatening (►**Fig. 3**).

Treatment Goals

Based on these guiding principles, treatment goals for claudicants should focus on the following[21]:

- Reducing risk of CV events through secondary prevention, using medical management of risk factors.
- Improving symptoms of claudication preventing substantial burden of functional decline in PAD and mobility loss using exercise and pharmacological interventions.
- The role of revascularization in claudication should be focused at improvement in claudication symptoms and functional status, and consequently in quality of life, rather than limb salvage.

How Do I Incorporate This into My Clinical Care of the Claudicant?

An individualized approach is recommended to optimize outcome, after a clear discussion with each patient.[13,22]

- A customized care plan that also includes medical therapy and structured exercise (section A below) represents the cornerstone of treatment of the claudicant.
- Revascularization (section B below) is reasonable in the following circumstances:
  - Inadequate response to optimal medical treatment (including structured exercise therapy).
  - Lifestyle-limiting claudication: this is defined as impairment of activities of daily living/vocational/recreational activities due to claudication.
  - Comorbid conditions like angina, respiratory diseases preventing use of optimal conservative measures.
  - Favorable risk/benefit ratio: revascularization is invasive, costly, and associated with risks. Patient preferences and goals of care are important considerations in the evaluation for revascularization, including realistic understanding of the durability of proposed procedures.

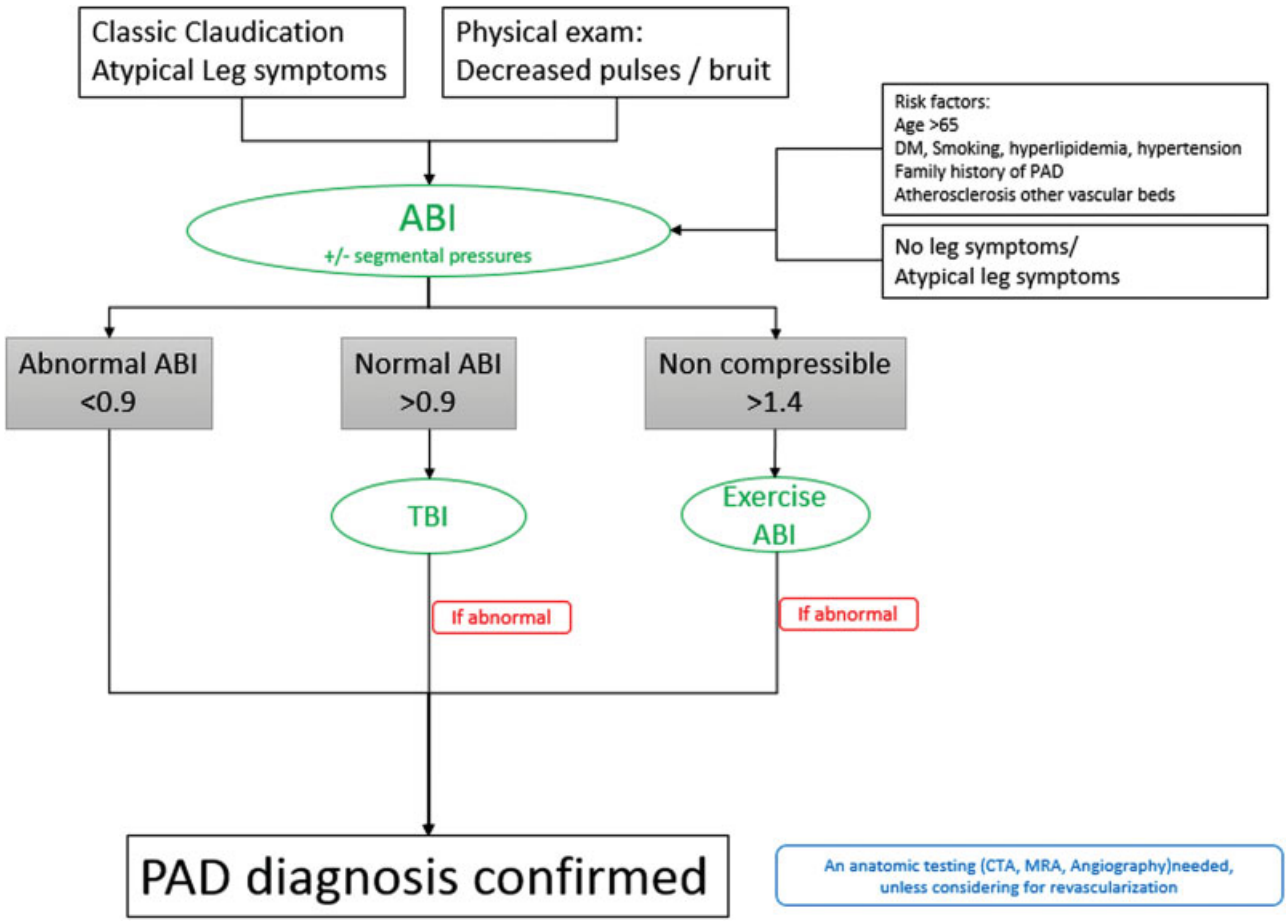

Fig. 1 Basic approach to making a diagnosis of PAD. ABI, ankle-brachial index; PAD, peripheral arterial disease.

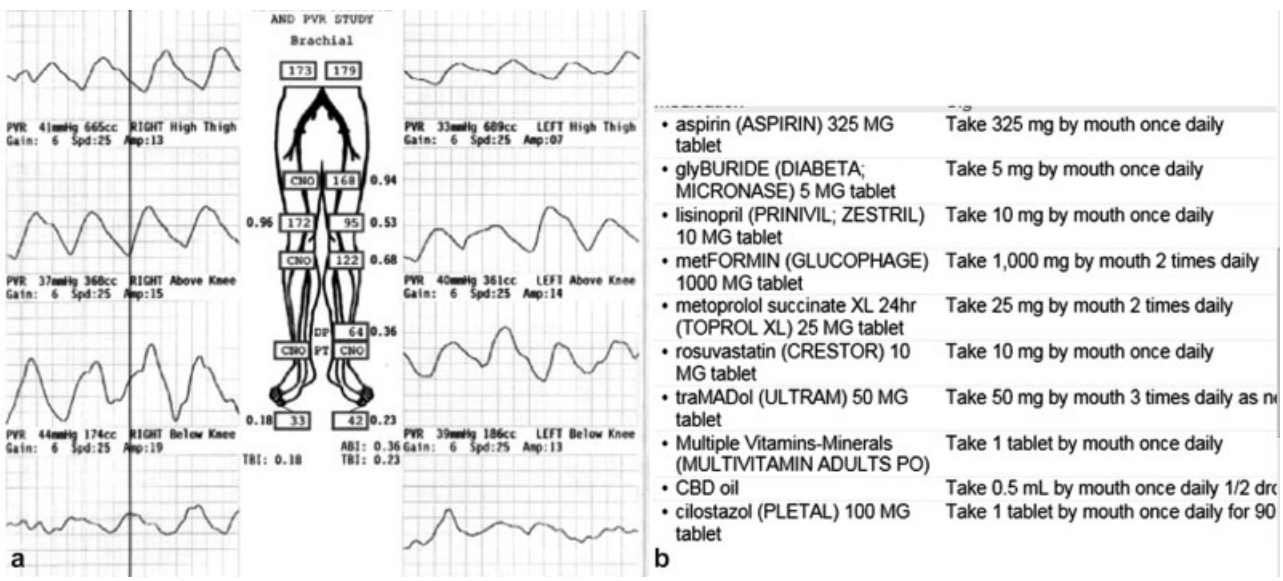

Fig. 2 A 70-year-old male with coronary artery disease s/p coronary artery bypass grafting and stenting, aortic valve replacement, hypertension, and diabetes mellitus presented with leg cramping after walking for ~5 minutes mainly on the treadmill; pain improves with rest. Patient has been attempting graduated exercise and he feels that improves the pain. Ankle-brachial index (ABI) was performed (**a**) which showed decreased ABI (left −0.36, greater than right). Patient was placed on optimal medical therapy (**b**) including cilostazol and advised home-based exercise therapy. Three months later, he reported improved claudication symptoms.

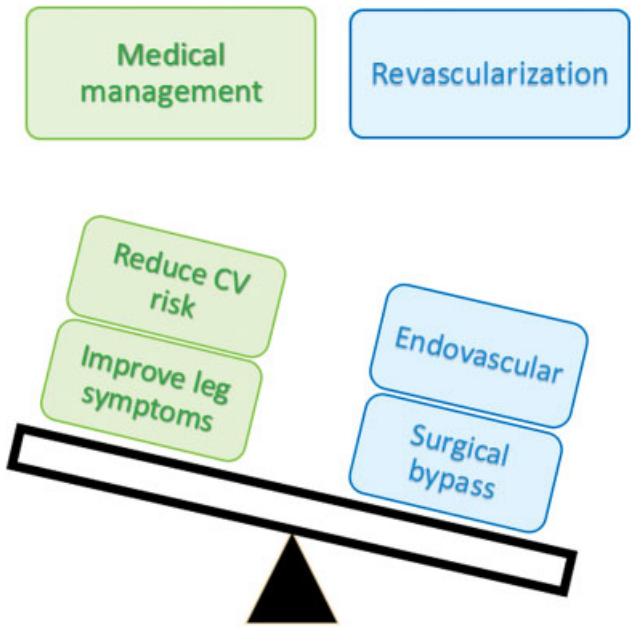

Fig. 3 The importance of medical management versus revascularization in the management of peripheral arterial disease.

►**Fig. 4** is a handy flowchart providing a framework of the decision process involved in treating a claudicant.

A. Medical Treatment

Medical treatment for PAD aims at measures to reduce the CV risk and leg symptoms.

i. Reducing the CV risk.
Medical management to reduce CV events includes smoking cessation, antiplatelet agents, statin therapy, blood pressure modification, and glucose control.[13,15,23] ►**Table 1** is a practical guide to medical treatment.
ii. Improving leg symptoms.

Exercise

The CLEVER (Claudication: Exercise Vs Endoluminal Revascularization) trial found that a supervised exercise program improved treadmill walking performance more than endovascular revascularization for patients with aortoiliac disease. Furthermore, both exercise and stent revascularization had better 18-month outcomes than optimal medical care.[24–26] The intermittent bouts of rest and exercise are thought to improve oxygen extraction by the muscles.

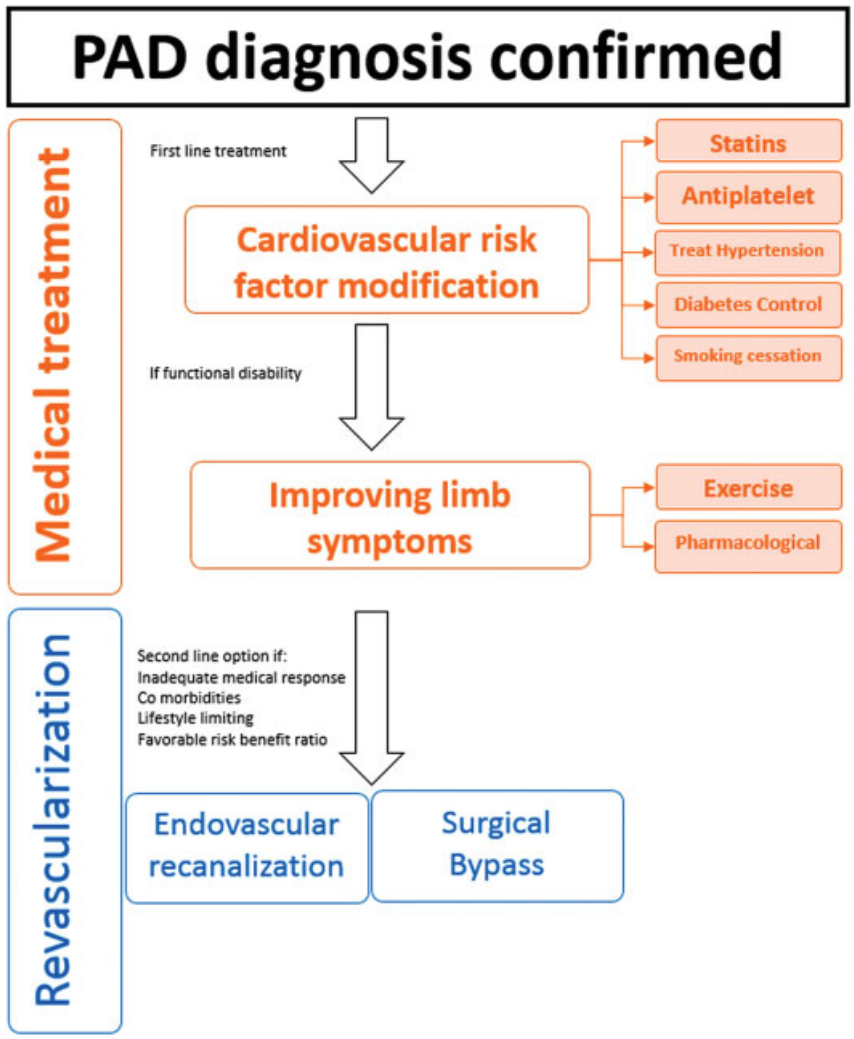

Fig. 4 Flowchart providing a framework of the decision process involved in treating a claudicant.

Table 1 Practical guide to medical treatment of claudicants

Patient situation	What to do	Evidence (AHA guidelines 2016)	Practical points
Not on antiplatelet therapy	Add single-antiplatelet agent: Aspirin: 81 mg/d Clopidogrel: 75 mg/d	A single-antiplatelet agent is recommended to reduce MI, stroke, and vascular death in patients with symptomatic PAD (level 1A)	Antiplatelet therapy also recommended in asymptomatic patient with ABI <0.9 Dual-antiplatelet therapy may be considered in patients who are extremely high risk (diabetes who smokes and concomitant CAD)
Not on statins	Add statin: Atorvastatin: 40 or 80 mg daily (or 10–20 mg if aged >75) Rosuvastatin (20 or 40 mg daily)	A statin medication is indicated for all patients with PAD, irrespective of cholesterol levels (level 1A)	Adverse effects (myalgia/myopathy) are typically mild and reversible. If this occurs, a lower dose of the same or alternative statin can be prescribed. Maximum dose of rosuvastatin is 10 mg if creatinine clearance is <30 mL/min
If hypertensive	Add antihypertensive agent: ACEI or ARB Ramipril: 2.5–20 mg/d Telmisartan: 20–80 mg/d	Antihypertensive therapy recommended to reduce the risk of cardiovascular events (level 1A)	Ideal target blood pressure remains an active topic of debate, new AHA guidelines SBP < 130 mm Hg
If diabetic	Refer to primary care/ endocrinology	Management of diabetes mellitus should be coordinated between members of the healthcare team (level 1C)	Meticulous foot care is of paramount importance
If smoker	Advice to quit and development of a strategy for cessation: Pharmacotherapy: consider varenicline, bupropion, and/or nicotine replacement therapy Smoking cessation program: refer to program, five "As" of smoking cessation are ask, advise, assess, assist, and arrange	Patients with PAD who smoke cigarettes should be advised to quit at every visit (level 1A)	Varenicline: More effective than bupropion and nicotine replacement therapy black-box warning for the psychiatric side effects does not exist Regimen: Days 1–3: 0.5 mg PO qd Days 4–7: 0.5 mg PO BID Day 8 to end of treatment: 1 mg PO BID If quitting is successful after 12 wk, continue another 12 wk at 1 mg q12h

Abbreviations: ABI, ankle-brachial index; ACEI, angiotensin-converting enzyme inhibitors; AHA, American Heart Association; ARB, angiotensin-receptor blockers; CAD, coronary artery disease; PAD, peripheral arterial disease; SBP, systolic blood pressure.

Exercise also improves endothelial function, blood pressure, cholesterol, glycemic control, and overall functional capacity.[27]

Although supervised exercise therapy provides significant symptomatic benefit for patients with claudication, it remains an underutilized tool, mainly due to lack of facilities and funding. A recent decision by the Centers for Medicare and Medicaid Services to cover supervised exercise for people with symptomatic PAD will, however, increase access to exercise for the large number of people disabled by PAD.[28] Structured community- or home-based exercise programs with an observation component (e.g., exercise logbooks, pedometers) are alternatives,[29] and can be used in special situations such as severe CV disease, amputation or wheelchair confinement, and other major comorbidities that would preclude exercise.[30] ►**Table 2** is a guide to the exercise regimen.

Pharmacological Treatment

Cilostazol is a selective phosphodiesterase III inhibitor and an effective therapy to improve symptoms and increase walking distance in patients with claudication.[31,32] Although there is an increase in adverse side effects like headache, diarrhea, palpitations, and lightheadedness, these are generally mild and treatable. Cilostazol should not be used in patients with history of heart failure.[31,33] ►**Table 3** includes a brief description of important information about the use of cilostazol.

B. Revascularization: Endovascular versus Surgical

Endovascular

Endovascular techniques to treat claudication include balloon dilation (angioplasty), stents, and atherectomy. These techniques continue to evolve and new technologies, including cutting balloons, drug-coated balloons, and drug-eluting stents to improve patency, but comparative effectiveness trials,

Table 2 A guide to the exercise regimen for claudicants

	Supervised exercise program	Structured community- or home-based exercise program
What is it?	Exercise directly supervised by qualified healthcare provider(s)	Exercise self-directed with guidance of healthcare providers
Where is it done?	Hospital or outpatient facility, typically walk on a motorized treadmill	Personal setting of the patient
How to do it?	Walk period: walk until development of claudication (usually moderate) Rest period: rest until subsidence of leg pain Alternating walk–rest periods for a 30–45 min/session	Exercise regimen (duration, intensity, frequency) similar to supervised. Patient counseling to ensure understanding of how to begin and maintain the program May incorporate behavioral change techniques, such as health coaching or use of activity monitors, exercise logbooks, pedometers
What is the frequency?	At least 3 times/wk for a minimum of 12 wk	At least 3 times/wk for a minimum of 12 wk
Advantages	Structured and effective	More practical personal setting of patients Offers alternatives (upper-body ergometry, cycling, and pain-free or low-intensity walking) for major comorbidities and wheelchair confinement
Drawbacks	Lack of facilities Lack of funding Difficult for patients who cannot exercise due to major comorbidities and wheelchair confinement	Not structured

are still pending.[34] ►**Fig. 5** shows a patient who underwent revascularization for lifestyle-limiting claudication.

Surgical Revascularization

Femoral-popliteal bypass is one of the most common surgical procedures for claudication. Autologous vein grafts have better long-term patency when compared with prosthetic materials for above-knee bypasses. In the long term (2–5 years), there was low-quality evidence that Dacron confers a small secondary patency benefit over PTFE for above-knee bypass.[35]

Which One? Endovascular versus Bypass Surgery

When revascularization is needed for patients with claudication, a decision of endovascular versus surgery should be made. Guidance on the revascularization strategy has traditionally been based on the complexity and location of disease as described in the TransAtlantic Inter-Society Consensus (TASC) II document.[36] Longer lesions and more complex disease are associated with higher rates of restenosis and poor long-term patency.[37,38] Although the anatomic subset delineation of TASC is useful, advances in technology now increasingly allow routine revascularization of TASC C and D lesions, in experienced hands.[13] Although patency outcomes for surgical bypass may be superior, these interventions are also associated with greater risk of adverse perioperative events as compared with the less invasive endovascular treatments. Treatment selection should therefore be individualized on the basis of the patient's goals, perioperative risk, and comorbid conditions.[13] ►**Table 4** includes a decision-making guide to choose endovascular recanalization versus bypass.

Table 3 Brief description of important information about the use of cilostazol

	Cilostazol
Mechanism of action	Phosphodiesterase III inhibitor Antiplatelet agent + vasodilator + smooth muscle antiproliferative + improvement in lipid profile
Dose	100 mg twice daily 30 min before or 2 h after a meal
Side effects	Common (20%) patients—headache, diarrhea, palpitations, and lightheadedness Mild and treatable
Contraindication	Cardiac failure

Conclusion

Optimal medical management goals for claudication include reducing CV morbidity and mortality and improving quality of life (►**Table 5**). Aggressive risk factor modification includes smoking cessation, antiplatelet therapy, a statin, an angiotensin-converting enzyme inhibitor, and treatment of underlying diabetes and hypertension. Exercise is highly effective for improving claudication symptoms. Pharmacological therapy with cilostazol may be considered for symptomatic treatment. Revascularization in claudication is focused at improvement in claudication symptoms and functional status, rather than aggressive attempts at limb salvage.

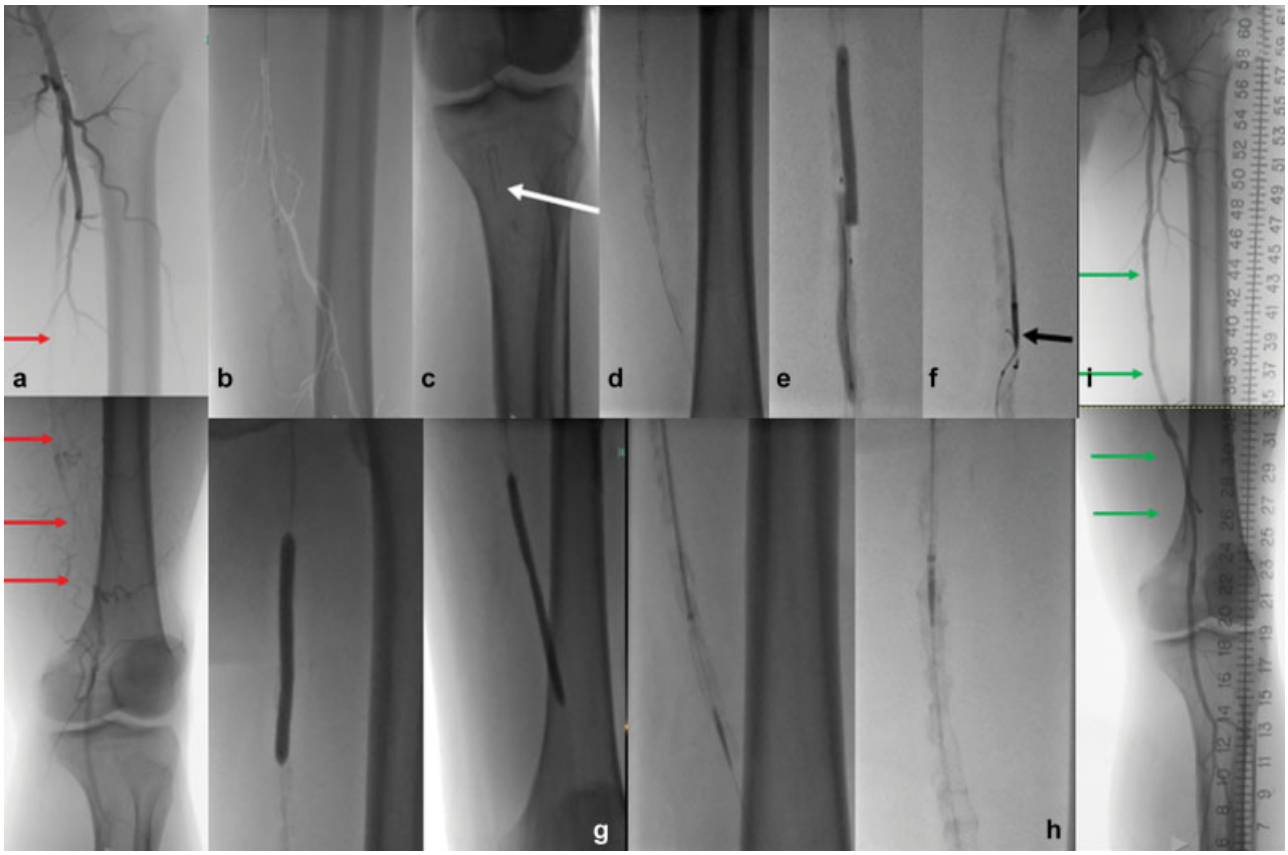

Fig. 5 A 64-year-old male with diabetes mellitus and hypertension presenting with lifestyle-limiting claudication in left leg. Ankle-brachial index in left leg was 0.35 (normal >0.9). Three-month trial of medical management, exercise therapy, and cilostazol failed to relieve symptoms. Endovascular revascularization was performed. (**a**) Initial angiography from contralateral femoral approach showed a long segment chronic total occlusion (CTO) involving the superficial femoral artery (SFA). (**b**) Multiple attempts at antegrade crossing failed. (**c**) A V18 (Boston Scientific) wire seen (*white arrow*) from a retrograde pedal access. (**d**) Antegrade and retrograde wires crossing most of the CTO, however, could not be connected. (**e**) Double-balloon technique from antegrade and retrograde access was also not successful. (**f**) A reentry device was useful to gain intraluminal access and a body floss was achieved by snaring the antegrade wire into the retrograde pedal sheath. (**g**) Balloon angioplasty of the entire CTO performed using a 6 mm × 100 mm balloon followed by placement of (**h**) two 6.5 mm × 80 mm nitional interwoven stents. (**i**) Post treatment angiogram showed recanalized SFA with good flow distally. At 3 month follow up patient had complete resolution of claudication.

Table 4 Decision-making guide to choose endovascular recanalization versus bypass

	Endovascular	Surgical
TASC lesions	TASC A and B	TASC C and D
Location of lesion:	Preferred approach for aortoiliac disease—long-term patency	Preferred in femoropopliteal disease—numerous complex 3D forces that are associated with restenosis
Lesion characteristics: number, length, severity	Preferred for short lesions, stenosis	Preferred for longer lesions, occlusion rather than stenosis, extensive calcification, diffuse lesions, poor-quality runoff
Patient comorbidities	Preferred approach	Less preferred, higher risk of postoperative events

Abbreviation: TASC, TransAtlantic Inter-Society Consensus.

Table 5 Important take-home points in the management of claudication

Take-home points:
• PAD is a prevalent, morbid, and mortal disease
• Implications of PAD derive from both its limb and cardiovascular manifestations
• Medical modification of cardiovascular risk factors and exercise are the cornerstone in the treatment of claudication
• Revascularization in claudication is focused at improvement in claudication symptoms and functional status, rather than aggressive attempts at limb salvage

Abbreviation: PAD, peripheral arterial disease.

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